Remarks

Prior to this amendment, claims 1-9, 11-13, 15-33 and 46-59 were pending in this application. Claims 1-10, 26-33 and 46-54 are currently withdrawn. Claims 11-13, 18-20, 23, 55, and 57-59 are amended herein. New claim 60 is added. Claims 1-9 and 15-17 are canceled herein without prejudice.

Claims 13, 20, 58, and 59 are amended to change dependency. Support for the amendment of claims 11 and 23 can be found in the specification at least at page 27, lines 24-26 and in original claim 17. Support for the amendment of claim 12 can be found in the specification at least at page 49, lines 20-23 and page 82, lines 8-9. Support for the amendment of claim 13 can be found in the specification at least at page 47, lines 1-9. Support for the amendment of claim 19 can be found in the specification at least at page 28, lines 1-2 and in original claim 20. Support for the amendment of claims 20, 58, and 59 can be found in the specification at least at page 27, line 32 through page 28, line 1. Support for the amendment of claim 55 can be found in the specification at least at page 64, lines 25-30. Support for the amendment of claim 57 can be found in the specification at least at page 77, lines 21-32 and page 83, lines 5-15. Support for new claim 60 can be found in the specification at least at page 28, lines 1-2 and at page 64, lines 12-14.

No new matter has been added in this amendment. Unless specifically stated otherwise, none of these amendments are intended to limit the scope of any claim. Applicants reserve the right to pursue any removed subject matter in a related application. After entry of this amendment, **claims 11-13, 18-33 and 46-60 are pending** (of which claims 26-33 and 46-54 are withdrawn).

Examiner Interview

Applicants thank Examiner Leavitt for the courtesy of a telephone interview with their representative Dr. Anne Carlson, on October 6, 2009. Although agreement was not reached on the final language of the claims, Applicants believe that the claims submitted herewith are in accordance with the telephone interview.

Withdrawal of Claim Rejections

Applicants thank Examiner Leavitt for withdrawing the rejections of claims 12 and 14.

Maintained Rejections under 35 U.S.C. 103

Claims 11-13, 15-25, 55, and 57 continue to be rejected, and claims 58-59 are newly rejected, under 35 U.S.C. 103(a) as allegedly being unpatentable over Radziejewski *et al.* (U.S. Patent No. 6,022,694) in view of Lipford *et al.* (U.S. Published Patent Application No. 2003/0148316). Applicants respectfully disagree. Claims 15-17 are canceled herein, rendering the rejection of these claims moot.

The claims are directed to a method of inducing maturation of an immature macrophage or an immature dendritic cell that expresses DDR1 (claim 11), or a method of producing an antigen presenting macrophage or dendritic cell (claim 23), by contacting the cells with a DDR1-activating antibody.

(a) The cited references

Radziejewski *et al.* discloses COS cells transfected with a nucleic acid molecule encoding DDR1 and the phosphorylation of the DDR1 receptor when DDR1-expressing cells are stimulated with collagen (column 15, lines 24-43 and column 17, lines 30-47). Radziejewski *et al.* also discloses that collagen is used to support the growth, survival, or differentiation of DDR1-expressing cells (column 4, lines 32-34). Radziejewski *et al.* does not disclose immature macrophages, immature dendritic cells, or DDR1-activating antibodies. Nor does Radziejewski *et al.* disclose a method of inducing maturation of an immature macrophage or an immature dendritic cell that expresses DDR1 (claim 11), or a method of producing an antigen presenting macrophage or dendritic cell (claim 23), by contacting the cells with a DDR1-activating antibody.

Lipford *et al.* (U.S. Published Patent Application No. 2003/0148316, filed on August 1, 2002; hereinafter the '316 publication) discloses that DDR1 (also referred to as Accession No. U48705 and CD167a) is up-regulated in dendritic cells during immunostimulation with CpG oligonucleotides (Table 5c). The '316 publication also discloses the use of agents, such as

antibodies, that modulate dendritic cell activity following exposure to an immunostimulatory nucleic acid (paragraph [0053]; claim 42). The '316 publication claims the benefit of U.S. Provisional Application No. 60/309,260 (hereinafter the '260 application; filed August 1, 2001). Examiner Leavitt noted that page 183 of Appendix B, which was submitted with the '260 application on August 1, 2001, discloses that DDR1 is expressed in immature dendritic cells and "[a]ccordingly, the effective filing date for the DDR1 marker in dendritic cell[s] is Aug. 1, 2001" (Office action at page 6). However, Applicants respectfully point out that page 183 of Appendix B also discloses that CpG immunostimulation had "no effect" on the DDR1-expressing cells.[1] Thus, the data in the '316 publication showing that CpG immunostimulatory nucleic acids up-regulate DDR1 is not supported by the disclosure of the '260 application. Moreover, unlike the '316 publication, the '260 application does not disclose antibodies that can modulate dendritic cell activity (such as DDR1-activating antibodies or antibodies that induce the maturation of immature macrophages or immature dendritic cells) or any agent that activates DDR1.

(b) The rejection in view of the cited references

As discussed above, the claims are directed to a method of inducing maturation of an immature macrophage or an immature dendritic cell that expresses DDR1 (claim 11), or a method of producing an antigen presenting macrophage or dendritic cell (claim 23), by contacting the cells with a DDR1-activating antibody.

Radziejewski *et al.* discloses that collagen activates DDR1-expressing COS cells. Radziejewski *et al.* does not disclose immature macrophages, immature dendritic cells, or a DDR1-activating antibody. Applicants respectfully submit that there is no specific teaching in Radziejewski *et al.* that an agent other than collagen (and certainly not an anti-DDR1 antibody) can be used to activate a DDR1-expressing cell. In addition, there is no specific teaching in Radziejewski *et al.* that collagen or any other agent could be used to induce the maturation of an immature macrophage or dendritic cell expressing DDR1, or to produce an antigen presenting macrophage or dendritic cell. Collagen is a completely different protein, structurally and functionally, from an antibody. In addition, COS cells, which are African Green Monkey

[1] According to page 9, lines 24-25 of the '260 application, Appendix B "markers are characterized as either increased, decreased or not (or negligibly) affected by CpG immunostimulation."

fibroblasts transformed with the SV40 virus, are completely different cells from immature macrophages and immature dendritic cells. Thus, one of skill in the art, would not have predicted, based upon the teachings of Radziejewski *et al.* alone, that an anti-DDR1 antibody (rather than collagen) could be used to (i) induce the maturation of an immature macrophage or immature dendritic cell expressing DDR1 (claim 11), or to (ii) produce an antigen presenting macrophage or dendritic cell (claim 23) (rather than activate a DDR-1-expressing COS cell).

Applicants had conceived of the idea to use an anti-DDR1 antibody to activate DDR1 prior to the August 1, 2002 filing date of the '316 publication (Lipford *et al.*) and diligently reduced the invention to practice less than two weeks after the August 1, 2002 filing date (see the Declaration of Prior Invention Under 37 C.F.R. 1.131 submitted with the Amendment and Response on April 14, 2009). Applicants thank Examiner Leavitt for acknowledging Applicants' prior invention in the current Office action. In view of the above discussion, Applicants respectfully submit that the '316 publication is not prior art and cannot be combined with Radziejewski *et al.*

The '316 publication claims the benefit of the '260 application (filing date August 1, 2001), which discloses that DDR1 is expressed on dendritic cells. However, as in Radziejewski *et al.,* there is no teaching in the '260 application that an agent can activate DDR1 expressed on a dendritic cell or that such an agent can be used to induce maturation of an immature macrophage or an immature dendritic cell that expresses DDR1 (claim 11), or can be used in a method of producing an antigen presenting macrophage or dendritic cell (claim 23). Moreover, the '260 application does not disclose DDR1-activating antibodies and fails to disclose *any agent* that affects (increases or decreases) DDR1 activity. Thus, one of skill in the art, would not have predicted, even when looking at the combined teachings of Radziejewski *et al.* and the '260 application, that an anti-DDR1 antibody could be used to activate DDR1 and induce the maturation of an immature macrophage or an immature dendritic cell that expresses DDR1, or could be used in a method of producing an antigen presenting macrophage or dendritic cell.

Accordingly, the combination of Radziejewski *et al.* and the '260 application does not render claims 11 and 23 obvious. Claims 12, 13, 18-25, 55-59 depend, directly or indirectly,

from claim 11 or 23 and incorporate all the limitations thereof. In view of the above discussion, Applicants submit that claims 11-13, 18-25, and 55-59 are non-obvious. Reconsideration and withdrawal of this rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. §112, first paragraph – New Matter

Claims 12, 13, and 57 are rejected as allegedly failing to comply with the written description requirement. Applicants respectfully disagree.

Claims 12 and 13 are rejected because the claims recite an "agent that up-regulates the expression of DDR1" or "agent that up-regulates DDR1 expression," respectively, and the Office action alleges that a "review of the specification as filed reveals no specific disclosure of up-regulation of DDR1 on immature dendritic cells or immature macrophages . . . Note that dendritic cells and macrophages are not monocytes or lymphocytes." Applicants respectfully disagree. Monocytes are, in fact, immature macrophages and immature dendritic cells (see, for example, the specification at page 13, lines 8-16; page 19, lines 28-29l page 74, lines 8-24) and can be derived from peripheral blood mononuclear cells (PBMC). Moreover, the specification clearly discloses that DDR1 mRNA (see page 47, lines 1-8) and protein (see page 49, lines 9-23) levels are up-regulated in immature macrophages or immature dendritic cells derived from PBMC when the cells are incubated in the presence of GM-CSF, tumor necrosis factor-α, interleukin-1β, lipopolysaccharide, phytohemagglutinin, or fetal calf serum, and that up-regulation of DDR1 is detected on the surface of the cells by an antibody that recognizes DDR1 (see page 82, lines 5-9). Thus, Applicants respectfully submit that claims 12 and 13 are fully supported by the specification.

Claim 57 is rejected for reciting "up-regulates chemokines or cytokines" because allegedly "there is nothing to lead one of skill in the art to appreciate that contacting an immature dendritic cell or immature macrophage expressing DDR1 with a DDR1-activating agent up-regulates chemokines or cytokines by a genus of undefined methods (*e.g.,* up-regulation of mRNA expression, cell surface protein expression, or protein secretion)" (Office action at page 10). Applicants respectfully disagree. The specification clearly describes a nexus between the activation of DDR1 with a DDR1-activating antibody and the up-regulation of cytokines and

chemokines secreted into the cell medium. For example, the specification describes that the measure of increased (up-regulated) levels of the secreted cytokines and chemokines could be readily detected by enzyme-linked immunosorbent assay (ELISA) (page 77, lines 21-32; page 83, lines 5-15). Thus, Applicants respectfully submit that claim 57 is fully supported by the specification.

In view of the above discussion, Applicants respectfully request reconsideration and withdrawal of this rejection of claims 12, 13, and 57.

Conclusion

Based on the foregoing arguments, the claims are in condition for allowance and notification to this effect is requested. If for any reason the Examiner believes that a telephone conference would expedite allowance of the claims, please telephone the undersigned at the number listed below.

Respectfully submitted,

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